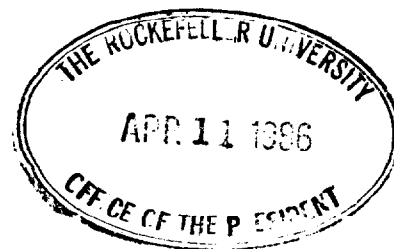




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Dear Dr. Lederberg:

Some years ago when you were at Stanford University, you led out in what appears to me to be a landmark contribution in Fundamental Chemistry. I refer to the calculation of the number of isomers which a molecule might have given its constituent atoms. I have been able to obtain some information about the results of this work, including the article "The Scope of Structural Isomerism," by Dennis H. Smith, and two articles by L. M. Masinter\* from a series on artificial intelligence.

I have a desperate need to find information on the number of possible isomers for as many molecules as possible. This need exists in order to clarify an important feature for the periodic system which we believe can be constructed for molecules with any given number of atoms. The periodic system for diatomic molecules has been extensively demonstrated to agree with the data and to allow the prediction of new data. Work on the periodic system for triatomic molecules has begun. As the number of atoms in the molecule increase, the problem of isomers grows more and more important - hence this letter.

The articles by Masinter\* give the number of isomers for a few molecules. The article by Smith gives the number of isomers for a large number of molecules, but

\*et al.

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unfortunately the numbers of hydrogen atoms are not listed (the degree of unsaturation is listed). I know that, in principle, it should be possible to reconstruct the molecular formula including the number of hydrogens with the tabulated information. However, our time and expertise are limited and so I am writing to see whether you might have the original print-outs in which the number of isomers are listed for the specific molecules including the exact number of hydrogen atoms. I venture to take your time for this question because of the invitation at the end of Dr. Smith's article.

Your attention to this question and any assistance you might be able to render (such as to whom to write for the necessary information) are deeply appreciated.

Respectfully yours,



Ray Hefferlin,  
Professor of Physics

RH'lh

such plots display a slightly decreasing slope with increasing carbon number for each given unsaturation.

As unsaturation increases, the slopes of the curves increase sharply (see Figure 1 as  $U$  increases from zero to four). However, curves representing higher unsaturation counts frequently begin, and remain for a short time below curves representing lower unsaturation counts, for example, the curves for  $U = 3$  and  $U = 4$ , Figure 1. It seems clear that the higher the degree of unsaturation the greater the possible number and combinations of multiple bonds and ring systems. This factor is responsible for increasing slope with increasing  $U$  observed in Figure 1. But, carrying this argument to its extreme, why should not the number of isomers for a given combination of atoms always be greater for higher unsaturation counts, as long as the total valence of the composition list can support the specified unsaturation? The next section discusses this point in more detail.

**The Number of Structural Isomers vs. Unsaturation Count.** In Figure 2 some selected data from Table I are plotted including various combinations of six atoms. This figure illustrates the typical rise and fall of the number of isomers with increasing unsaturation. The value of unsaturation at which the number of isomers reaches a maximum is a complex function of the number and identity of atoms. The value shifts slowly to higher values of unsaturation as the number of atoms increases. Most composition lists of four atoms show maxima at  $U = 1$  or 2. Several composition lists of six atoms have maxima at  $U = 3$ . However, most still display maxima at  $U = 1$  or 2.

It is interesting to note that there is a smooth variation of number of isomers with unsaturation. No example presented in Table I shows a number of isomers which declines, then rises again with increasing unsaturation.

The curves presented in Figure 2 serve to introduce another set of questions and observations. These are concerned with the effects on the number of isomers caused by replacement of one type of atom with another type.

**The Number of Structural Isomers vs. Atom Type.** Most chemists intuitively expect that a given number of atoms and unsaturations will yield a larger number of isomers when a more diverse collection of atoms. As a first approximation, this is true, as indicated in Figure 2. The curve of  $C_4N_2H_2$  lies above the curve of  $C_4$  for all values of  $U$ ; the curve of  $C_4O_2$  lies above that of  $C_4$  for  $0 \leq U \leq 4$ . It is reasonable to expect that, in a comparison of the results of exchange of atom type (e.g., either one N or one O for one C), the exchange yielding a higher total valence results in a group of atoms capable of yielding a greater diversity of structures. To a first approximation this is also true, as the curve of  $C_4N_2$  lies above that of  $C_4O_2$  for all values of  $U$  (Figure 2).

Results presented previously, however, indicate the subtle interplay of atom type and valence. Intuition often fails to predict the relative numbers of isomers resulting from replacing an arbitrary number of atoms by the same number of atoms which differ in name and valence. Some representative data selected from Table I are presented in Table II to bring out the influence of variation of atom type on the number of isomers.

For a given unsaturation count, the ratio between numbers of isomers resulting from N-substitution vs. O-substitution increases with increasing substitution, e.g.,  $N_2O_2$ ,  $N_3O$ ,  $N_4O$ , Table II.

## DISCUSSION

The variations of numbers of isomers with increasing numbers of atoms, with unsaturation count or with substitution of one atom type with another can be rationalized on the same basis. Knowledge of an algorithm for constructing structural isomers, such as that used by the structure gen-

Table I. Structural Isomers of  $C_xN_yO_z$ ,  $x + y + z \leq 6$ , for Allowed Values of the Unsaturation,  $U$

No. of atoms	Unsaturation							
	0	1	2	3	4	5	6	7
$C_6$	1							
$C_5O$	1	1						
$C_5N$	1	2	1	1				
$C_4O_2$	2	5	9	11	7	3		
$C_4N_2$	3	10	26	40	40	21	6	
$C_4O$	5	25	77	159	217	185	85	19
$C_3O_3$	1							
$C_3O_2N$	1	1						
$C_3O_2$	2	3	3	1				
$C_3ON_2$	3	9	13	9	2			
$C_3O_2N_2$	7	26	55	62	36	7		
$C_3O_2$	14	74	205	337	318	151	21	
$C_2O_4$	1	1						
$C_2O_3N$	2	2	1					
$C_2O_3$	5	10	9	3				
$C_2ON_2$	11	34	52	34	7			
$C_2O_2N_2$	28	122	263	361	163	28		
$C_2O_2$	1	1						
$C_2ON$	3	4	1					
$C_2O_2N_2$	10	22	20	5				
$C_2O_2$	28	102	152	98	16			
$C_2ON_2$	1	1						
$C_2O_2N_2$	5	6	2					
$C_2O_2$	20	48	41	10				
$C_2ON_2$	1	1						
$C_2O_2N_2$	6	9	2					
$C_2O_2$	1	1						
$C_2ON$	1	1	1					
$C_2O_2N_2$	2	4	5	2				
$C_2O_2$	4	12	21	19				
$C_2ON_2$	8	35	55	55	7	2		
$C_2O_2N_2$	17	100	313	503	305	15	1	
$C_2ON_2$	1	1	1					
$C_2O_2N_2$	2	4	4	1				
$C_2O_2$	6	18	27	19	5			
$C_2ON_2$	14	62	136	155	88	11		
$C_2O_2N_2$	38	218	632	1008	1005	407	61	
$C_2ON_2$	1	2	1					
$C_2O_2N_2$	4	11	13	6				
$C_2O_2$	14	58	110	98	34			
$C_2ON_2$	45	259	681	969	706	131		
$C_2O_2N_2$	3	4	4	2				
$C_2O_2$	8	26	47	31	6			
$C_2ON_2$	37	189	439	512	272	43		
$C_2O_2N_2$	2	7	9	4				
$C_2O_2$	15	73	145	151	42			
$C_2ON_2$	4	15	25	15	6			
$C_2O_2N_2$	1	1						
$C_2O_2$	3	5	3					
$C_2ON_2$	8	22	26	11				
$C_2O_2N_2$	21	84	154	153	46			
$C_2O_2$	56	260	761	1002	718	210		
$C_2ON_2$	2	3	1					
$C_2O_2N_2$	9	21	18	4				
$C_2O_2$	31	115	177	114	20			
$C_2ON_2$	102	527	1194	1671	703	88		
$C_2O_2N_2$	3	7	4					
$C_2O_2$	21	71	86	21				
$C_2ON_2$	101	481	935	1006	250			
$C_2O_2N_2$	6	18	17	4				
$C_2O_2$	52	225	361	267	32			
$C_2ON_2$	11	43	55	22				
$C_2O_2N_2$	2	2						
$C_2O_2$	8	15	8					
$C_2ON_2$	28	84	99	40				
$C_2O_2N_2$	90	391	732	641	201			
$C_2O_2$	5	8	3					
$C_2ON_2$	28	75	63	12				
$C_2O_2N_2$	132	521	807	506	76			
$C_2O_2$	10	23	13					
$C_2ON_2$	86	306	369	157				
$C_2O_2N_2$	24	72	66	14				
$C_2O_2$	3	3						
$C_2ON_2$	17	34	18					
$C_2O_2N_2$	76	246	283	110				
$C_2O_2$	9	15	5					
$C_2ON_2$	73	207	175	29				
$C_2O_2N_2$	24	58	30					
$C_2O_2$	4	4						
$C_2ON_2$	33	68	34					
$C_2O_2N_2$	17	27	8					
$C_2O_2$	5	5						